NON-TECHNICAL ABSTRACT

High-Dose Chemotherapy and Autologous Bone Marrow plus Peripheral Blood Stem Cell Transplantation for Patients with Lymphoma or Metastatic Breast Cancer: Use of Marker Genes to Investigate the Biology of Hematopoietic Reconstitution in Adults.

PRINCIPAL INVESTIGATOR: **Dan Douer, MD**

This protocol is intended for patients with breast cancer or lymphoma who will be treated by autologous bone marrow transplantation (BMT) to restore their bone marrow function that has been previously damaged by high doses of chemotherapy drugs. The bone marrow is the site where all blood cells are produced from cells that we call "stem-cells". Because the high doses of chemotherapy will destroy these normal blood producing cells (stem-cells), transplantation of the previously collected bone marrow (which contains stem-cells) is necessary. We know that the blood also contains a few stem cells, which can be collected then transplanted together with the bone marrow cells. It is believed that by adding blood stem cells to the bone marrow cells, the recovery of bone marrow function after the transplantation is faster. However, we do not know if these circulating blood stem cells are different from the bone marrow stem cells, or if they are also capable of permanently renewing the bone marrow function. We also do not know if a few invisible cancer cells may be still present in the transplanted bone marrow or blood and whether they contribute differently to recurrence of cancer after being infused back into the patient.

To answer these questions, we will insert a gene into some of the bone marrow and a slightly different gene into some of the blood cells. A special laboratory technique will be used to put the genes into a portion of the bone marrow and a portion of the blood which were previously collected. These treated bone marrow and blood cells are referred to as "marked" cells. By inserting these particular genes into the cells, we will be able to distinguish the marked cells from all other cells in the body. If any of the blood cells and marrow cells that return after the transplantation contain the cells that are marked by the gene, we would be able to follow these markers over a long period of time. We then would know if the blood stem cells or bone marrow stem cells were responsible for permanent marrow function after the transplantation. In addition, if the cancer re-occurs, and one or both of the genes is present in the recurring tumor, we may be able to determine if invisible tumor cells were actually present in the bone marrow or blood, perhaps contributing to the relapse of cancer after transplantation. In this clinical trial, 10 patients with lymphoma or breast cancer will be studied.

The introduction of these genes would have no treatment benefit to the patient but the results may lead to a better understanding as to how the bone marrow and blood stem-cells recover after transplantation and also may help to plan better ways to improve the safety and usefulness of this procedure.

No side effects have been seen in animals or any person treated thus far with these marker genes. Consequently, for the several patients who have already received these genes, no side effects ("toxicity") have been observed.